APPLICANTS: Baker et al. DOCKET NO: ISIS-5300 SERIAL NO: 10/701.265

AMENDMENTS TO THE CLAIMS: This listing of claims replaces all prior versions and listings of claims in the instant patent application.

What Is Claimed Is:

1-119. (canceled)

120. (new) A composition comprising a duplex consisting of a first chemically synthesized oligomeric compound and a second chemically synthesized oligomeric compound, wherein:

each of the first chemically synthesized oligomeric compound and the second chemically synthesized oligomeric compound independently consists of 17 to 25 linked nucleosides, each nucleoside comprising a nucleobase and a sugar;

at least 17 contiguous nucleobases of the first chemically synthesized oligomeric compound are 100% complementary to at least 17 contiguous nucleobases of the second chemically synthesized oligomeric compound;

the first chemically synthesized oligomeric compound and the second chemically synthesized oligomeric compound are not covalently linked to each other; and

the first chemically synthesized oligomeric compound is a gapmer, wherein the gap comprises at least 4 nucleosides, each comprising a 2'-OH, and wherein each nucleoside of each wing comprises a 2' modification or is an LNA nucleoside.

- 121. (new) The composition of claim 120, wherein the second chemically synthesized oligomeric compound is a gapmer, wherein the gap comprises at least 4 nucleosides, each comprising a 2'-OH, and wherein each nucleoside of each wing comprises a 2' modification or is an LNA nucleoside.
- 122. (new) The composition of claim 120, wherein the duplex comprises an overhang on the 5' end, on the 3' end, or on both the 5' end and the 3' end.
- 123. (new) The compound of claim 120, wherein the duplex is blunt-ended.

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- 124. (new) The composition of claim 120, wherein each nucleoside of at least one of the wings of the gapmer comprises a 2' sugar modification selected from fluoro, alkoxy, amino-alkoxy, allyloxy, imidazolylalkoxy, and methoxyethoxy or is an LNA nucleoside.
- 125. (new) The composition of claim 120, wherein each nucleoside of one wing of the gapmer comprises a 2'-fluoro and each nucleoside of the other wing of the gapmer comprises a 2'-OCH₃.
- 126. (new) The composition of claim 120, wherin each nucleoside of the 5' wing of the gapmer comprises a 2'-fluoro.
- 127. (new) The composition of claim 120, wherein each nucleoside of the 3' wing of the gapmer comprises a 2'- OCH₃.
- 128. (new) The composition of claim 126, wherein each nucleoside of the 3' wing of the gapmer comprises a 2'- OCH₃.
- 129. (new) The composition of claim 128, wherein the first chemically synthesized oligomeric compound is a sense strand.
- 130. (new) The composition of claim 128, wherein the first chemically synthesized oligomeric compound is an antisense strand.
- 131. (new) The composition of claim 120, wherein each nucleoside of one wing of the gapmer comprises a 2'-fluoro and each nucleoside of the other wing of the gapmer is an LNA.
- 132. (new) The composition of claim 120, wherein each nucleoside of the 3' wing of the gapmer is an LNA.
- 133. (new) The composition of claim 126, wherein each nucleoside of the 3' wing of the gapmer is an LNA.
- 134. (new) The composition of claim 133, wherein the first chemically synthesized oligomeric compound is a sense strand.

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135. (new) The composition of claim 133, wherein the first chemically synthesized oligomeric compound is an antisense strand.

- 136. (new) The composition of claim 120, wherein each wing of the gapmer is from two to seven nucleosides in length.
- 137. (new) The composition of claim 120, wherein at least one of the first chemically synthesized oligomeric compound and the second chemically synthesized oligomeric compound comprises at least one phosphorothioate linkage.
- 138. (new) The composition of claim 137, wherein each of the first chemically synthesized oligomeric compound and the second chemically synthesized oligomeric compound comprises at least one phosphorothioate linkage.
- 139. (new) A compound comprising a chemically synthesized oligomeric compound, wherein:

the chemically synthesized oligomeric compound consists of 17 to 25 linked nucleosides, each nucleoside comprising a nucleobase and a sugar;

the chemically synthesized oligomeric compound is a gapmer, wherein the gap comprises at least 4 nucleosides, each comprising a 2'-OH, and wherein each nucleoside of each wing comprises a 2' modification or is an LNA nucleoside; and

the chemically synthesized oligomeric compound is an antisense compound.

- 140. (new) The compound of claim 139, wherein each nucleoside of at least one of the wings of the gapmer comprises a 2' sugar modification selected from fluoro, alkoxy, amino-alkoxy, allyloxy, imidazolylalkoxy, and methoxyethoxy or is an LNA nucleoside.
- 141. (new) The compound of claim 139, wherein each nucleoside of one wing of the gapmer comprises a 2'-fluoro and each nucleoside of the other wing of the gapmer comprises a 2'-OCH₃.
- 142. (new) The compound of claim 139, wherein each nucleoside of the 5' wing of the gapmer comprises a 2'-fluoro.

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- 143. (new) The compound of claim 139, wherein each nucleoside of the 3' wing of the gapmer comprises a 2'- OCH₃.
- 144. (new) The compound of claim 142, wherein each nucleoside of the 3' wing of the gapmer comprises a 2'- OCH₃.
- 145. (new) The compound of claim 139, wherein each nucleoside of one wing of the gapmer comprises a 2'-fluoro and each nucleoside of the other wing of the gapmer is an LNA.
- 146. (new) The compound of claim 139, wherein each nucleoside of the 3' wing of the gapmer is an LNA.
- 147. (new) The compound of claim 142, wherein each nucleoside of the 3' wing of the gapmer is an LNA.
- 148. (new) The compound of claim 139, wherein each wing of the gapmer is from two to seven nucleosides in length.
- 149. (new) The compound of claim 139, wherein the chemically synthesized oligomeric compound comprises at least one phosphorothioate linkage.
- 150. (new) A composition comprising a duplex consisting of a first chemically synthesized oligomeric compound and a second chemically synthesized oligomeric compound, wherein:

each of the first chemically synthesized oligomeric compound and the second chemically synthesized oligomeric compound independently consists of 17 to 25 linked nucleosides, each nucleoside comprising a nucleobase and a sugar;

at least 17 contiguous nucleobases of the first chemically synthesized oligomeric compound are 100% complementary to at least 17 contiguous nucleobases of the second chemically synthesized oligomeric compound;

the first chemically synthesized oligomeric compound and the second chemically synthesized oligomeric compound are not covalently linked to each other; and APPLICANTS: Baker et al. SERIAL NO: 10/701,265

the first chemically synthesized oligomeric compound is a blockmer comprising at least one region comprising at least 4 contiguous nucleosides, each comprising a 2'-OH, and a block region, wherein each nucleoside of the block comprises a 2' modification or is an LNA nucleoside.

- 151. (new) The composition of claim 150, wherein the second chemically synthesized oligomeric compound is a blockmer comprising at least one region comprising at least 4 contiguous nucleosides, each comprising a 2'-OH, and a block region, wherein each nucleoside of the block comprises a 2' modification or is an LNA nucleoside.
- 152. (new) The composition of claim 150, wherein the duplex comprises an overhang on the 5' end, on the 3' end, or on both the 5' end and the 3' end.
- 153. (new) The compound of claim 150, wherein the duplex is blunt-ended.
- 154. (new) The composition of claim 150, wherein each nucleoside of the block of the blockmer comprises a 2' sugar modification selected from fluoro, alkoxy, amino-alkoxy, allyloxy, imidazolylalkoxy, and methoxyethoxy or is an LNA nucleoside.
- 155. (new) The composition of claim 150, wherein the first chemically synthesized oligomeric compound is a sense strand.
- 156. (new) The composition of claim 150, wherein the first chemically synthesized oligomeric compound is an antisense strand.
- 157. (new) The composition of claim 150, wherein the block is from two to seven nucleosides in length.
- 158. (new) The composition of claim 150, wherein the block is at the 3' terminal end of the chemically synthesized oligometric compound.
- 159. (new) The composition of claim 150, wherein the block is at the 5' terminal end of the chemically synthesized oligomeric compound.

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160. (new) The composition of claim 150, wherein at least one of the first chemically synthesized oligomeric compound and the second chemically synthesized oligomeric compound comprises at least one phosphorothioate linkage.

- 161. (new) The composition of claim 150, wherein each of the first chemically synthesized oligomeric compound and the second chemically synthesized oligomeric compound comprises at least one phosphorothioate linkage.
- 162. (new) A compound comprising a chemically synthesized oligomeric compound, wherein:

the chemically synthesized oligomeric compound consists of 17 to 25 linked nucleosides, each nucleoside comprising a nucleobase and a sugar;

the chemically synthesized oligomeric compound is a blockmer comprising at least one region comprising at least 4 contiguous nucleosides, each comprising a 2'-OH, and a block region, wherein each nucleoside of the block comprises a 2' modification or is an LNA nucleoside; and

the chemically synthesized oligomeric compound is an antisense compound.

- 163. (new) The compound of claim 162, wherein each nucleoside of the block of the blockmer comprises a 2' sugar modification selected from fluoro, alkoxy, amino-alkoxy, allyloxy, imidazolylalkoxy, and methoxyethoxy or is an LNA nucleoside.
- 164. (new) The compound of claim 162, wherein the block of the blockmer is from two to seven nucleosides in length.
- 165. (new) The compound of claim 162, wherein the block of the blockmer is at the 5' end of the chemically synthesized oligomeric compound.
- 166. (new) The compound of claim 162, wherein the block of the blockmer is at the 3' end of the chemically synthesized oligomeric compound.
- 167. (new) The compound of claim 162, wherein at least one of the chemically synthesized oligomeric compound comprises at least one phosphorothioate linkage.